WP1 Enabling Chemistries

The sustainability of future chemical manufacturing processes will rely on the delivery of novel synthetic routes. Taking a 'process-driven' approach, WP1 seeks to exploit emerging technologies to overcome hurdles in the discovery, processing and scaling-up of new flow reactions, to reduce waste, energy consumption and CO_2 emission. We will focus on key chemical transformations that are important and relevant in the agrochemical and pharma sectors; i.e. the development of synthetic capabilities for highly valuable molecules with moderate to high complexity. In particular, reactions that are currently not possible or unsafe to be implemented in batch reactors, including photo- and electro-chemical reactions that can replace energy-inefficient or thermally-inaccessible pathways.

Improve selectivity (OF1). A selective process is inherently efficient, as it minimises, if not eliminating, the competitive formation of side-products. By improving product quality, less downstream process is required to remove impurities, which not only lower capital and operating costs, but also improved sustainability. A continuous flow process can deliver products with higher quality more consistently, by offering better control of temperature, mixing, pressure and residence time. Equally, the precise control of residence time is particularly beneficial for accessing thermally sensitive moieties, which cannot be made in batch, e.g. by rapidly heating a reaction mixture, before it is (thermally) quenched to minimise product decomposition. Accordingly, reactive intermediates can be generated safely *in situ* and utilized immediately to afford excellent selectivity.

Non-thermal activation (OF2). The chemical industry is the largest energy consumer and third largest emitter of CO_2 in the manufacturing sector. Thermally-enabled reactions have a large carbon footprint as it typically requires gas/fossil fuels for heating and it is generally difficult to maintain a high temperature and recover it through heat integration without losses. Moreover, many desired products degrade at high temperature, compromising yield and selectivity. Hence, alternatives to thermal activation are essential to meet sustainability goals. Non-thermal activation processes such as photo- and electro-chemical reactions are not only potentially less energy intensive, the reactive intermediates generated tends to be short-lived single-electron species which has very different, or complementary, reactivity and selectivity to thermally-induced reactions, affording new synthetic pathways to novel chemical entities. Reactions that can be activated by photons and electrons often proceed at ambient conditions, and can be achieved, in principle, by utilising (renewable) solar or electrical energies, respectively. Both photo- and electro-chemistries have witnessed a resurgence in interest in recent years, due to the direct utilization of renewable electricity, the availability of energy-efficient LED-light and new electrode materials (e.g. boron-doped diamond) that can deliver high photo- and current-efficiencies. These reactions would benefit from flow chemistry, as transfer of photons or electrons to the molecules can be facilitated under controlled mixing and isothermal conditions.

Screening & optimization (OF3). In this programme, the discovery of new reactions will be augmented by automated experiments to derive reaction understanding (mechanism) and control (kinetics), which will eventually lead to better reaction and reactor designs. Building upon the state-of-the-art reaction analytics available in the ROAR facility, systematic screening and optimization of the process parameters (e.g. temperature, pressure, residence times, concentrations, mixing) and reaction parameters (e. g. substrates, reagents, solvents, catalysts) will be incorporated as an essential part of the discovery workflow. This approach will support a deeper mechanistic understanding and modelling of a comprehensive reaction kinetic network, e.g. through the combination of model-based design of experiment with self-optimizing systems. *OF3* includes the development of self-optimizing flow systems as a standard tool-kit to realize a step change in R&D methodology; by accelerating the exploration of reaction scope and windows, leading to reduced development cost, and shorter time-to-market.